Allergol Immunopathol (Madr). 2017;xxx(xx):xxx-xxx

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

www.elsevier.es/ai

ORIGINAL ARTICLE

Serum periostin is not related to asthma predictive index

J.A. Castro-Rodriguez*, I. Atton, G. Villarroel, C.A. Serrano

Division of Pediatrics, School of Medicine, Pontificia Universidad Catolica de Chile, Santiago, Chile

Received 29 April 2017; accepted 19 May 2017

KEYWORDS
Asthma;
Asthma predictive index;
Periostin;
Pre-school;
Recurrent wheezing

Abstract
Background: In contrast to adult asthmatic patients, studies on the role of serum periostin levels in schoolchildren with asthma are still conflictive, and very few studies have been performed in pre-schoolers. The aim of this study was to compare serum periostin levels in recurrent wheezer pre-schoolers according to their asthma predictive index (API) condition.
Methods: We performed a case-control study enrolling pre-schoolers with recurrent wheezing episodes (>3 episodes confirmed by physician) presented at one paediatric clinic in Santiago, Chile. The population was divided according to stringent API criteria into positive or negative.
Results: In a one-year period, 60 pre-schoolers were enrolled. After excluding 12 (due to not fulfilment of inclusion criteria or refusal of blood sample extraction), 48 remaining pre-schoolers (27 males, age range from 24 to 71 months) completed the study; 34 were API positive and 14 were API negative. There were no significant differences in demographics between groups. The level of serum periostin levels for pre-schoolers with positive API and negative API were (median 46.7 [25.5-83.1] and 67.5 [20.5-131.8], $p = 0.9$, respectively). The area under the curve for the serum periostin levels for predict positive API was 0.5, 95% CI [0.29-0.70], $p = 0.9$. No significant correlation between serum periostin levels and peripheral blood eosinophils was found.
Conclusion: Serum periostin levels were no significantly different between wheezer pre-schoolers with positive and negative API. More studies are needed to confirm this finding.

Introduction

Asthma is one of the most common chronic diseases in children.[1] Recurrent wheezing in pre-school age is frequently the presenting sign of asthma; however, many

* Corresponding author.
E-mail address: jacastro17@homail.com
(J.A. Castro-Rodriguez).

https://doi.org/10.1016/j.aller.2017.05.012
0301-0546/

Please cite this article in press as: Castro-Rodriguez JA, et al. Serum periostin is not related to asthma predictive index. Allergol Immunopathol (Madr). 2017. https://doi.org/10.1016/j.aller.2017.05.012

children who wheeze during early life do not go on to develop childhood asthma.[1] Based on the epidemiological data on the natural history and temporal patterns of wheezing, several childhood wheezing phenotypes have been described. However, the use of these ''epidemiological'' phenotypes of wheezing is limited, since they can only be identified retrospectively; indeed, they were defined using statistical inference on longitudinally collected data, and are not useful in the present as they are defined by events that will occur in the future.[2]

To solve that problem, in the past decades, several asthma predictive rules have emerged.[3] The Asthma Predictive Index (API)[4] uses only clinical parameters (paternal asthma, rhinitis, dermatitis, wheezing without cold and eosinophils in peripheral blood) is the most widely used and the only one that fulfils all the steps for clinical prediction rules,[5] e.g. development,[4] validation/updating,[6–8] impact[9–12] and implementations.[13–16] The API which is related with atopic asthma inception is simple and cheap, and its major strength is its good positive likelihood ratio ~7.4 and high specificity (~97%).[17]

Peripheral blood eosinophils have been identified as a surrogate marker of type 2 inflammation. These particular cells are considered the main effector cell in the pathophysiology of asthma.[18] High levels of peripheral blood eosinophils are recognised as an important biomarker for the eosinophilic asthma phenotype and have been identified as a readily available biomarker that correlates with disease severity and may predict response to asthma therapy.[19,20]

Periostin is a matricellular protein whose expression can be induced by type 2 inflammatory cytokines IL-4 and IL-13, as well as by other stimuli such as TGF-beta. IL-13 induces the secretion of periostin from bronchial epithelial cells.[21] Periostin is secreted basally from airway epithelial cells where it has pleotropic effects on epithelial cell function and on the development of airway fibroblasts, which is thought to promote airway remodelling in asthmatic patients. An in vitro study showed that airway epithelial cells from schoolchildren with allergic asthma express higher levels of periostin than cells from children without asthma.[22] Periostin levels in peripheral blood have been identified as an easily obtained systemic biomarker of type 2 airway inflammation in adults and may also predict responsiveness to therapy (e.g. inhaled corticosteriods, lebrikizumab).[21,23]

However, the literature on serum periostin levels in asthmatic children is scarce and conflictive. For example, one study on schoolchildren suggests that elevated serum periostin level correlates with airway hyperresponsiveness, whereas another found that high periostin level was not a predictor of asthma morbidity.[24,25] Moreover, only one study was performed at pre-school age reporting that those who developed asthma by age six years had increased serum periostin at age two years, in comparison to those who did not develop asthma by age six years.[26]

The objective of this study is to assess if pre-schoolers with recurrent wheezing episodes and positive API differ in serum periostin levels than those with negative API, and if peripheral eosinophils correlate with serum periostin levels in this particular age group. Our hypothesis is that pre-schoolers with positive API would have higher serum periostin levels than those with negative API.

Methods

In this case–control study, a convenience sample of sixty-two pre-schoolers (2–5 years of age) with recurrent wheezing episodes (more than three episodes/year) who consulted in the outpatient paediatric clinic at Pontificia Universidad Catolica de Chile were recruited from March 2015 to March 2016. The study was previously approved by the Ethical Committee at the Pontificia Universidad Catolica de Chile (# 14-048). Informed consent was obtained from the parents or legal guardians before patient inclusion.

The inclusion criteria were: recurrent wheezing (≥3 episodes per year with diagnosis by a paediatrician) without inhaled corticosteroids (ICS) treatment in the last month and without leukotriene receptor antagonist (LTRA) in the last two weeks. Exclusion criteria were patients with other chronic respiratory illness, e.g. cystic fibrosis, bronchopulmonary dysplasia, post-infection bronchiolitis obliterants, cardiac or pulmonary malformations, and acute respiratory infection in the last three weeks.

A detailed questionnaire was completed and collected at enrolment. It included demographic characteristics, parental history of asthma and allergic diseases, rhinitis, atopic dermatitis, history of wheezing episodes, onset and their severity, cough at night and after exercise, parental higher educational degree, exposure to tobacco smoke, and day-care attendance. On the same day, a peripheral blood sample was obtained to assess eosinophil counts and serum periostin levels. Serum was stored at −20 °C before measurement of periostin level. Periostin was determined by ELISA (Human Periostin/OSF-2 ELISA Kit, Wuhan City, China) and expressed as ng/mL.

Using the data from the questionnaire and peripheral blood eosinophils count, patients were divided into two groups: positive API and negative API. We used the stringent API definition, e.g. positive API was considered if they had one major (parental MD asthma or MD eczema) or two minor criteria (MD allergic rhinitis, wheezing apart from colds or peripheral blood eosinophilia >4%).[4]

Statistical analysis

We compared pre-schoolers with positive API versus negative API. Continuous variables with normal distribution were described in mean ± standard deviation (SD), and compared using T-test. Continuous variables without normal distribution were described in median [25–75 percentile], and used non-parametric test (Mann–Whitney). Categorical variables were described in contingency tables and compared using chi2 with Fisher exact test. A bivariate risk analysis was performed by calculating odds ratio (OR) with 95% confidence interval (CI). Spearman's rho correlation between the serum periostin levels and peripheral blood eosinophils was performed. The receiver operational curve (ROC) analyses were performed to investigate the capacity of serum periostin levels to predict positive API. The overall accuracy of the test was measured as the area under the ROC curve. Statically significant differences were considered for a p value < 0.05. All statistical analyses were performed using GraphPad Prism V.5.

Please cite this article in press as: Castro-Rodriguez JA, et al. Serum periostin is not related to asthma predictive index. Allergol Immunopathol (Madr). 2017. https://doi.org/10.1016/j.aller.2017.05.012